News and Views from the Literature

Erectile Dysfunction

Pomegranate Juice: Is It the New, All-Natural Phosphodiesterase Type 5 Inhibitor?

Reviewed by Jacob Rajfer, MD

Department of Urology, University of California at Los Angeles, Los Angeles, CA

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Pomegranate juice, which is derived from the pomegranate fruit, has been shown to have potent antioxidants, supposedly even more than in wine or green tea. It has recently been shown that it seems to protect nitric oxide (NO) in its continuing battle against oxidative stress, and it thereby has the potential to enhance the effect of NO on certain biologic systems.[1] Because tumescence occurs as a result of an intact NO–cyclic guanosine monophosphate (cGMP) pathway within the cavernosal nerve and cavernosal smooth muscle cells, it seems logical to determine whether pomegranate juice can cause improvement in erectile function.

Efficacy and Safety of Pomegranate Juice on Improvement of Erectile Dysfunction in Male Patients With Mild to Moderate Erectile Dysfunction: A Randomized, Placebo-Controlled, Double-Blind, Crossover Study

Forest CP, Padma-Nathan H, Liker HR.

Int J Impot Res. 2007;19:564-567.

Forest and colleagues studied 60 sexually active, healthy men between 21 and 70 years of age who had erectile dysfunction (ED) for at least 3 months as determined by the International Index of Erectile Function questionnaire. Patients were randomized to either placebo or pomegranate juice. Pomegranate juice (8 oz) or placebo was taken daily at night for 28 days, outcomes were measured, and then there was a 2-week washout period followed by a crossover period in which pomegranate juice or placebo was given for another 28 days. A final outcome measurement was then performed. The bottom line is that daily pomegranate juice for at least 28 days did not improve one's erection regardless of whether one was in the first or second treatment group. This study highlights the fact that not all bench findings prove clinically efficacious and demonstrates the necessity of randomized, double-blind, placebo-controlled studies. The authors are to be congratulated for publishing these negative but important findings.

Daily Phosphodiesterase Type 5 Inhibitor for Erectile Dysfunction: Is It Ready for Prime Time?

The phosphodiesterase type 5 (PDE-5) inhibitors are an unusual class of drugs because they upregulate the effect of cGMP, which itself is activated by NO. Upregulation of cGMP has been shown to inhibit both collagen synthesis and apoptosis of certain parenchymal cells, such as those found in the kidney and the corporal tissues. We in urology are most familiar with the fact that these drugs are classically used for the treatment of ED and are taken on demand when an erection is desired. However, many of the disorders that afflict the genitourinary tract have to do with loss of smooth muscle cells and/or increase in tissue collagen or fibrosis. Examples of these are overactive bladder (OAB), benign prostatic hyperplasia (BPH), and even aging-related ED, in which there is a loss of corporal smooth muscle cells and an increase in tissue fibrosis.

Therefore, it seems reasonable that if PDE-5 inhibitors are antifibrotic and antiapoptotic, they may be considered for the prevention of certain urologic disorders rather than for the on-demand treatment of ED.[2] However, this would require that they be taken on a daily basis and possibly early on in life, as one would take a statin or aspirin to prevent certain cardiovascular diseases.

Evaluation of the Efficacy and Safety of Once-a-Day Dosing of Tadalafil 5 mg and 10 mg in the Treatment of Erectile Dysfunction: Results of a Multicenter, Randomized, Double-Blind, Placebo-Controlled Trial

Porst H, Giuliano F, Glina S, et al.

Eur Urol. 2006;50:351-359.

To determine whether the daily ingestion of a PDE-5 inhibitor would be safe, Porst and colleagues performed a study in which men with ED were randomized to either placebo (n = 54), tadalafil 5 mg (n = 109), or tadalafil 10 mg (n = 105) daily for 12 weeks. The investigators found that besides the expected efficacy of the drug in men with ED, the side effect profile was no different than that seen with men taking those dosages of the drug on an on-demand basis. Only 8 of the 214 patients (3.7%) who took tadalafil reported an adverse event that precipitated their withdrawal from taking the drug daily. There was a dose-dependent increase in headaches (6.4% to 10.5%), dyspepsia (5.5% to 11.4%), back pain (3.7% to 9.5%), upper abdominal pain (2.8% to 8.6%), and myalgias (2.8% to 6.7%) in the patients taking tadalafil.

This study opens the way for testing these drugs over the long term in the treatment of some of the aforementioned urologic disorders. Sildenafil, another PDE-5 inhibitor, is currently approved as a daily treatment for pulmonary hypertension, and it does not seem far-fetched that in the future a PDE-5 inhibitor could be one of the drugs, like aspirin for cardiovascular disease, that is taken daily to prevent or delay the onset of certain aging-related urologic disorders, such as OAB, BPH, and even ED. In addition, because the penis is the window to what is occurring within the cardiovascular system, it is also plausible that these drugs may play a role in the treatment of certain cardiovascular disorders, such as heart failure and arteriosclerosis. ■

References

1. Ignarro LJ, Byrns RE, Sumi D, et al. Pomegranate juice protects nitric oxide against oxidative destruction and enhances the biological actions of nitric oxide. *Nitric Oxide*. 2006;15:93-102.
2. Sandner P, Hutter J, Tinel H, et al. PDE5 inhibitors beyond erectile dysfunction. *Int J Imp Res*. 2007;19:533-543.

Male Fertility

When Is Azoospermia Not Azoospermia?

Reviewed by Jacob Rajfer, MD

Department of Urology, University of California at Los Angeles, Los Angeles, CA

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Men with azoospermia, defined as no sperm in the ejaculate as documented by semen analysis, either have an obstruction to the excretory ductal system or defective spermatogenesis. The observation that more than 60% of men with defective spermatogenesis may have pockets of spermatogenesis within the testis[1,2] provides hope that many of these "azoospermic" patients can potentially be fathers with testicular sperm extraction (TESE) or testicular sperm aspiration (TESA) together with intracytoplasmic sperm injection and in vitro fertilization, provided these "pockets" of sperm, which theoretically never make it out of the ductal system, can be successfully harvested. TESE in these nonobstructive azoospermic patients requires either the use of a microscope to find the sperm (micro-TESE) or multiple